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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/459,979	12/14/1999	MARK WILLIAM JAMES FERGUSON	39-196	1874

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EXAMINER
JIANG, DONG

ART UNIT	PAPER NUMBER
1646	28

DATE MAILED: 07/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/459,979	FERGUSON, MARK WILLIAM JAMES	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's amendment in paper No. 19, filed on 12 May 2003 is acknowledged and entered. Following the amendment, claims 39-43 are canceled, and the new claims 46-49 are added.

Currently, claims 46-49 are pending and under consideration.

Withdrawal of Objections and Rejections:

All objections and rejections of claims 39-43 are moot as the applicant has canceled the claims.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons applied for claims 39-43, set forth in the last Office Action, paper No. 18, mailed on 11 February 2003, at pages 3-4.

Applicants argument, filed on 12 May 2003 (paper No. 19) has been fully considered, but is not deemed persuasive for reasons below.

At page 5 of the response, the applicant argues that the presence of granulation tissue in chronic wounds is indicative of healing, and further argues at page 7 that "the skilled person would perceive that the ability of IFN-γ to increase inflammation and angiogenesis in 7 day and 14 day wounds (as described in the results reported at page 9 of the specification) indicates that IFN-γ is able to increase the strength of the wound healing response, and thereby promote healing of chronic wounds." Applicant further argues that scaring seen in 70 day and 120 day

wounds would be recognized as a consequence of the same increasing wound healing and fibrotic response, and to be desirable to induce in chronic wounds. This argument is not persuasive because applicant has not provided evidence that one of skill in the art would immediately recognize the increased inflammation, angiogenesis and scarring instantly disclosed as beneficial in the healing process of chronic wounds. The results on page 9 of the specification indicate that increased inflammation and angiogenesis was observed in a dose dependent manner in 7 day and 14 day treated wounds, and that increased scaring was seen in 70 day and 120 day treated wounds, however, the benefit of this response in treatment of chronic wounds is not set forth in the specification. Contrary to the proposal that one of skill would recognize the benefit of this response for chronic wound healing, the specification states "lower doses although *worse* than control wounds, were *not as bad* as wounds treated with higher doses of IFN-γ." This language would indicate that one of skill would interpret the application of IFN-γ as a wound healing aid to be negatively indicated, as implied by the language "worse" and "not as bad". Nowhere on page 9 (and into page 10) is the application of IFN-γ as a chronic wound healing therapy suggested. Applicants argument regarding enablement issue assessed base on "Wands" factors are addressed below.

With respect to the nature of the invention, applicants argue, at page 8 of the response, that the present invention lies in a field of the art in which a certain degree of experimentation, such as pilot studies and clinical trials, is *necessary* in order to meet statutory regulations, and that this requirement should be considered as a mitigating factor. This argument is not persuasive because, while certain routine experimentation, and even the expectation of further research and development such as Phase II clinical testing may be permissible under the patent law, the issue is that this is not the case here. The nature of the invention is extremely complex and unpredictable, as indicated by the specification and the prior art. On page 3 of the instant specification, it is stated "very surprisingly, the inhibition of IFN-γ actually promotes healing with reduced scarring, despite the teachings of the prior art". As set forth previously in this record, the role of IFN-γ in wound healing is controversial and complex. For instance, Badgett et al. (J. Lipid mediators Cell signaling, Jan. 1996, 13(1): 89-97) teaches that IFN-γ is known to prime macrophages for increased the production of PDGF, which is a potent mediator of

fibroblast proliferation and chemotaxis (the abstract, lines 1-2), however, on the other hand, in the presence of PDGF, IFN-γ block PDGF-induced fibroblast proliferation. Therefore, the net role of IFN-γ in fibroblast proliferation and chronic wound healing in vivo is unclear and complex.

With respect to the state of the prior art, applicants argue, at page 8 of the response, that at the time the invention was made, a wealth of information available to illustrate that increasing the magnitude of the wound healing response such as fibrosis was a positive indicator of healing in chronic wounds, and that the skilled person would have immediately appreciated the results in the instant application to be likely to have utility in promoting healing of chronic wounds. This argument is not persuasive because, even though fibrosis may be a positive indicator of healing in chronic wounds, the prior art discussed above indicates that IFN-γ blocks PDGF-induced fibroblast proliferation, which contradict the present assertion as to a positive role of IFN-γ in healing of chronic wounds.

With respect to the relative skill of those in the art, applicants argue, at page 9 of the response, that the skilled person would have immediately recognize that compounds capable of increasing scarring and fibrosis would make them suitable candidates for treatment of chronic wounds. This argument is not persuasive because of the contradictory teachings of the prior art, contradictory teachings of the present specification (as discussed above), and lack of supporting evidence in the specification as there is no working example of chronic wounds is provided. As such, one of skill in the art would be highly in doubt about the role of IFN-γ in healing of chronic wounds.

With respect to the level of predictability in the art, applicants argue, at pages 9-10 of the response, that those involved in research leading to novel clinical therapies are familiar with the need to extrapolate the results from animal experiments to a human clinical context, and that the skilled person would immediately appreciate the ability of IFN-γ to increase fibrosis in animal models of wound healing, and identify it as a compound likely to be useful in promoting healing of chronic wounds in humans. This argument is not persuasive because, while it is a common practice to extrapolate the results from animal experiments to a human clinical context, the real issue here is that the animal model provided in the specification represents acute wound healing,

but not chronic. Given the fact that acute and chronic wounds are distinct in their causes and mechanisms, pathological changes, clinical manifestation and process, and response to treatment, that the prior art has not established that the response of chronic wounds can be predicted from the results of treating acute wounds, and that [the present specification indicates that at the early time points, high dose IFN-γ seems to worsen the acute wound, it is extremely unpredictable how chronic wounds would respond to the treatment effective on acute wounds, and thus one may not extrapolate the results from animal experiments of acute wounds to a human clinical context of chronic wounds, as one cannot represent the other.

With respect to the existence of working examples, applicants argue, at page 10 of the response, that the instant specification provides clear description of treatment with IFN-γ, and the skilled person would readily appreciate the ability of IFN-γ to promote healing of chronic wounds. This argument is not persuasive because the example in the specification merely represents a model of acute wound healing, and the art has not established that acute wound is equivalent to, and indicative of chronic wound. Therefore, it cannot be used as evidence to support the claimed invention.

With respect to the amount of direction or guidance provided by the inventor, applicants argue, at page 12 of the response, that the instant specification provides detailed guidance as to suitable routes, times and amounts of IFN-γ, and ample direction and guidance to allow the skilled person to put the invention into practice. This argument is not persuasive because the specification provides no information as to how to treat chronic wounds, and with the statements in the specification, such as "*early* treatment of wounds [acute] with causes fibrosis with raised scars that are packed full of collagen" (page 10, the first paragraph), and "the invention will be further apparent from the following example which shows ... forms of *inhibition* of IFN-γ, and promoting of healing with reduced scarring, and of promotion of healing of chronic wounds " (page 6, the last paragraph), it is very confusing as to how and if would be effective for chronic wounds, which are "*late*" wounds.

With respect to the quantity of experimentation needed to make or use the invention, applicants argue, at page 13 of the response, that the instant application discloses the use of IFN-γ to promote wound healing in an animal model, and that the skilled person would accept that the

limited experimentation necessary to extrapolate the results from an animal model to the use in human therapies in no way represents an unnecessary burden. This argument is not persuasive because the issue is not whether one may extrapolate the results from an animal model to the use in human therapies, rather, the issue is that, as addressed above, one may not extrapolate the results from acute wound model to the use of chronic wounds, as one cannot represent the other. One of skilled in the art would have to generate a model of chronic wound, and test and determine the effect of IFN-γ, which, by no means, are *routine* experimentation, and they constitute *undue* experimentation.

In summary, giving the controversial teachings of the prior art and the instant application, and the lack of working example demonstrating that IFN-γ indeed promotes chronic healing, one of skill in the art would not instantly recognize the results set forth on page 9 of the specification to be equivalent to, and indicative of the healthy deposition of granulation tissue used as a measure of healing of chronic wounds in the OASIS and PUSH assays, especially in light of the contraindication set forth in the specification on pages 9 and 10, and the complexity of the art.

Conclusion:

No claim is allowed.

Advisory Information:

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Dong Jiang, Ph.D.
Patent Examiner
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7/21/03

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